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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
08/482402	06/07/98	HEPNEY R. WILSON	1841/0121

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EXAMINER

LINGAN, S

ART UNIT

PAPER NUMBER

1806

12

DATE MAILED: 01/21/98

1/21/98

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on 1/16/98

☐ This action is FINAL.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 11-15 + 37 is/are pending in the application.

Of the above, claim(s) 37 is/are withdrawn from consideration.

☐ Claim(s) is/are allowed.

☒ Claim(s) 11-15 is/are rejected.

☐ Claim(s) is/are objected to.

☐ Claim(s) are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number)

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received:

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

21 April 1998 - Response
21 May 1998 - Response F1
21 June 1998 - Response F2
21 July 1998 - Response F3
MINEXTENDABLE

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1. The Election filed January 16, 1997 (Paper No. 11) in response to the Office Action of August 7, 1997 (Paper No. 8) is acknowledged and has been entered. Claims 11-15 and 375 are pending in the application and Claim 37 has been withdrawn from further consideration by the examiner under 37 CFR 1.142(b) as being drawn to non-elected inventions. Claims 11-15 are pending and are currently under prosecution.
2. Applicant's election with traverse of Group I, claims 11-15 in Paper No. 11, filed January 16, 1998, is acknowledged. The traversal is on the ground(s) that the instant divisional application corresponds to Group IV of the four-way Restriction Requirement issued in the parent application and that the instant application claims the benefit under 35 USC 1.129(b)(1) and that therefore the Office is prohibited from maintaining the requirement for restriction of the instant application. The argument has been noted but has not been found persuasive because it was clearly stated in Paper No. 8, Section 3, pages 2-3, that the rules concerning the transition restriction provisions were published in the Federal Register at 60 FR 20195 (April 25, 1995) and in the Official Gazette at 1174 O.G. 15 (May 2, 1995) and that the transitional restriction provisions permit applicant to have more than one independent and distinct invention examined in the same application by paying a fee for each invention in excess of one. Further it was clearly stated that "Applicant must either: (1) elect the invention or inventions to be searched and examined and pay the fee set forth in 37 CFR 1.17(s) for each independent and distinct invention in excess of which applicant elects; or (2) file a petition under 37 CFR 1.129(b) traversing the

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requirement." Since neither a fee has been paid nor a petition filed, the restriction requirement is deemed to be proper and is therefore made FINAL.

Declaration

3. The oath or declaration is defective. A new oath or declaration in compliance with 37 C.F.R. § 1.67(a) identifying this application by its Serial Number and filing date is required. See M.P.E.P. §§ 602.01 and 602.02.

The oath or declaration is defective because:

The post office address of inventor Rapoport has been omitted, it must be supplied.

Specification

4. In the continuity data disclosed on page 1 of the specification, priority is claimed to PCT/US92/0731 and PCT/US92/06283. There is no indication of the Declaration that priority, under 35 USC 120, is being claimed for these PCT's. Either reference to these PCT's must be deleted or a new Declaration, claiming priority to these PCT's must be filed. Appropriate correction is required.

5. In the Brief Description of the Drawings, Informalities where Applicant does not refer to panels of the figures are too numerous to mention, for example on Page 12, in the description of Figure 7, panels A-F are not referred to or described. Examiner has made an effort to identify these informalities but applicant must carefully review the specification to identify and indicate where these informalities occur. Appropriate correction is required.

6. The Brief Description of the Drawings is disclosed on pages 11-16 and continued on pages 144-149. The Brief Description must be on consecutive

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pages and the specification must be amended to delete the "Figure descriptions continued at page 144" on line 13 of page 16, and the "Brief Description of the Drawings (continued from Page 16)" from lines 5 of page 144 through line 7 of page 149. A description of Figures 21-38 must be added at line 13 of page 16 and the entire specification must be appropriately repaginated. Appropriate Correction is required.

7. Each Figure of the drawings must be individually numbered, for example, Figure 22 is disclosed on two sheets and is labeled Fig. 22 and Fig 22 (Cont.). Informalities where Applicant labels drawings with a figure number and then figure number (Cont.) are too numerous to mention. Examiner has made an effort to identify these informalities but applicant must carefully review the specification to identify and indicate where on the drawings these informalities may be found. Further, Figure 31A is disclosed on two sheets and is labeled Fig. 31A and Fig 31A (Cont.). These must be renumbered Figure 31A and Figure 31B and the instant Figure 31B and 31C must be relabeled Figure 31C and Figure 31D. Furthermore the Brief Description of the Drawings and all references to the drawings in the specification must be amended to reflect the new numbering of the drawings.

8. The drawings submitted with this application were declared informal by the applicant. It is noted that the drawings as disclosed are not in consecutive order, for example, Fig 8 and Fig 5 are on the same sheet as are figures 21 and 28. When formal drawings are submitted, they must be submitted in consecutive numerical order.

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9. The Abstract of the Disclosure is objected to because the Abstract does not describe the invention as currently claimed. Correction is required. See M.P.E.P. § 608.01(b).

10. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

Claim Rejections - 35 USC § 112

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

"The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention."

12. The specification is objected to under 35 USC 112, first paragraph, and Claims 11-14 are rejected under 35 USC 112 first paragraph as failing to provide sufficient guidance to enable one skilled in the art to make/use a recombinant DNA sequence encoding human thyroid peroxidase which is secreted from a host cell.

(a) The disclosure appears to be enabling and descriptive only for claims limited to the secretable human thyroid peroxidase in which stop codons are present at nucleotide positions 2629-31 and 2641-43 and its production by CHO cells.

The specification discloses one working example of a DNA sequence encoding thyroid peroxidase, which when transfected into CHO cells, produces a

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truncated protein which is secreted from the host cells. It does not appear that this single example enables or describes each and every DNA sequence which would encode a secretable peroxidase and its production thereof.

The claims encompass any DNA sequence encoding a secretable human thyroid peroxidase, including deleted DNA sequences and DNA sequences which contain additional nucleotides. However applicant only teaches one sequence which encode a secretable protein. Applicant does not teach where else in the disclosed thyroid peroxidase a stop codon would produce a secreted form nor does applicant disclose whether the addition of a signal sequence, for example, would permit the secretion of said peroxidase. Absent further working examples and instructions, it could not be predicted from the disclosure that all shortened or lengthened thyroid peroxidase sequences would be stable produced and secreted by host cells, thus it would require undue experimentation, by one of skill in the art, in order to make/use the invention, as claimed.

(b) The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with the claims. The claims as written read on any possible cell. The specification gives no guidance on or exemplification of the production and secretion of thyroid peroxidase by any host cell other than CHO cells. There appears to be no basis in the specification for such broad claims. Applicant fails to disclose expression and secretion of thyroid peroxidase by bacteria, yeast, fungi, or any other cell type other than mammalian CHO cells. Since it is well known that the signals for nucleic acid

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translation and transcription, codon usage, and protein processing and targeting are not universally recognized by all classes or organisms, it could not be predicted that any thyroid peroxidase sequence would be produced and secreted by any host cell into which it was transformed, therefore undue experimentation would be required to enable the claims.

13. Claims 11-15 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(a) Claims 11-15 are indefinite because claim 11 recites "human thyroid peroxidase" which is indefinite because it fails to set forth the essential characteristics and aspects applicant intends to claim. For example, it is unclear whether applicant intends an antigenic or enzymatically active protein.

(b) Claims 11-15 are indefinite because claim 11 recites the phrase "recombinant DNA sequence encoding human thyroid peroxidase which is secreted from a cell" because it is unclear whether it is the DNA sequence or the protein encoded by the DNA sequence which is secreted from the cell.

(c) Claims 12 and 13 are indefinite because they recite the phrase "a stop codon upstream" but fail to set forth exactly how far upstream applicant intends said stop codon to lie. Note that a stop codon five amino acids after the start codon of the human peroxidase sequence would be upstream from the transmembrane domain.

Claim Rejections - 35 USC § 101

13. 35 U.S.C. § 101 reads as follows:

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"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

14. Claims 11-13 are rejected under 35 USC 101 because the claimed invention is directed to non-statutory subject matter.

The recombinant DNA sequence reads on DNA as it exists in nature. The claims fail to recite that the DNA is isolated or purified, thus indicating the "hand of man." For example, the claimed DNA sequences encompass naturally, arising mutations that exist in somatic cells.

Claim Rejections - 35 USC § 103

15. The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

16. Claims 11-15 are rejected under 35 USC 103 as being unpatentable over Seto et al (J. Clin. Invest., 1987, 80:1205-1208) or Libert et al (NAR, 1987, 15:6735) in view of Lee et al (Nature, 1981, 294:228-232) or Ellis et al (Cell, 1986, 45:721-732), EP 0139 417 or Rose et al (Cell, 1982, 30:753-762) and Magnusson et al (JBC, 1987, 262:13885-13888).

Seto et al teach the DNA sequence of human thyroid peroxidase

Libert et al teach the complete nucleotide sequence of thyroid peroxidase.

Although both Seto et al and Libert et al teach the complete nucleotide sequence of human thyroid peroxidase, neither Seto et al or Libert et al teach a recombinant DNA sequence encoding human thyroid peroxidase which is secreted from a cell with stop codons upstream from a transmembrane domain, a vector which comprises the DNA sequence or a host cell transformed with the vector.

EP 0139 417 teaches that deletion of the hydrophilic carboxyl-terminus of the gD protein results in its secretion into the media when recombinant cDNA encoding the truncated protein is transfected into host CHO cells (see page 11, lines 30-35 and pages 22-26). The advantages of secreted proteins are described (page 32, lines 1-15).

Rose et al teach that deletion of the hydrophobic, transmembrane, carboxyl-terminus of the G protein results in its secretion into the medium in which transformed cells are cultures.

Magnusson et al teach the structural gene for porcine thyroid peroxidase. Hydropathy analysis revealed a carboxyl-terminal transmembrane domain,

Extra
Cellular

G protein
is intracellular

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consistent with its cellular location that is a putative membrane anchor (page 13887).

Lee et al teach expression vectors containing DHFR and the MMTV promoter which are capable of expressing heterologous genes in CHO cells (see Fig 1).

Ellis et al teach an SV40 based expression vector, pECE, which is capable of expressing heterologous proteins in CHO cell lines (see Figures 1 and 3)

Since Magnusson et al. teach that thyroid peroxidase contains a carboxyl-terminal hydrophobic domain which is a putative membrane anchor (p. 13887, col 2, lines 2-6), it would have been expected that its deletion would result in a secretable protein in view of either EP 0 139 417 or Rose et al who teach that deletion of a carboxyl-terminal hydrophobic domain from a membrane-bound protein results in its secretion when transformed into a host cell. Absent new or unexpected results, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have deleted the hydrophobic, transmembrane region of the thyroid peroxidase sequence of either Seto et al or Libert et al for the purpose of producing a recombinant DNA sequence encoding human thyroid peroxidase that would produce a secretable recombinant protein whose known advantages are taught by EP 0 139 417.

Further, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have employed the expression vectors of either Lee et al or Ellis et al for the purpose of producing human thyroid peroxidase as a matter of experimental design in which one known gene

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as taught by Seto et al or Libert et al is substituted for another in order to produce the protein as taught by either Lee et al or Ellis et al. The selection of said vectors and thyroid peroxidase sequences would have been well within the purview of the ordinary skilled artisan since each would have been chosen for their known and expected properties.

In regard to the particular thyroid peroxidase sequence which is cloned and expressed, it would have been obvious to have selected other thyroid peroxidase sequences from the libraries of either Seto et al or Libert et al., employing the probes of either Set et al or Libert et al since such selection methods were well known at the time the invention was made.

9. No claims allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Ungar, PhD whose telephone number is (703) 305-2181. The examiner can normally be reached on Monday through Friday from 7:30am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lila Feisee, can be reached at (703) 308-2731. The fax phone number for this Art Unit is (703) 308-4242.

Communications via Internet e-mail regarding this application, other than those under 35 USC 132 or which otherwise require a signature may be used by the applicant and should be addressed to lila.feisee@uspto.gov.

All internet e-mail communications will be made of record in the application file. **PTO employees do not engage in Internet communications**

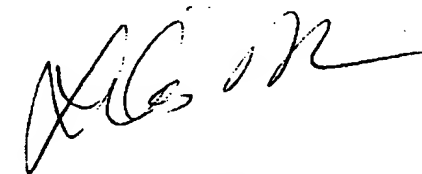
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where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of USC 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Susan Ungar

January 14, 1998



LILA FEISEE
SUPERVISORY PATENT EXAMINER
GROUP 1800